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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,105	10/04/2001	Ann Burchell	350013-76	4877

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/972,105	BURCHELL ET AL.
	Examiner	Art Unit
	Lisa V. Cook	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,9 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,9 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/392,055.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

10.0

DETAILED ACTION

1. Applicant's response to the office action mailed February 9, 2005 is acknowledged (paper filed 6/13/05). Currently, claims 2-7, 9, and 12-15 are under consideration.

2. Rejections and/or Objections of record not reiterated herein have been withdrawn.

OBJECTIONS WITHDRAWN

Drawings

3. The drawings in this application are objected to by the Draftsperson as informal. Any drawing corrections requested, but not made in the prior application should be repeated in this application if such changes are still desired.

If the drawings were changed and approved during the prosecution of the prior application, a petition may be filed under 37 CFR 1.182 requesting the transfer of such drawings provided the parent application has been abandoned. However, a copy of the drawings as originally filed must be included in the 37 CFR 1.60 application papers to indicate the original content.

Also, Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Applicants have submitted formal drawings in the response filed 6/13/05. Accordingly the objection to the drawings is withdrawn.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 2, 5-7, 9 and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al. (Prenatal Diagnosis, Vol.13, 293-300, 1993) in view of Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) and Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770).

Bianchi et al. teach a method of isolating fetal nucleated cells from maternal blood. An antigen present on the cell surface of the fetal erythrocyte is detected and related to a gene or gene portion associated with a disease or condition, a chromosomal abnormality or sex-specific DNA, in the maternal blood sample. See abstract.

Three different antibodies are utilized to separate the fetal nucleated erythrocytes (red blood cells) form maternal blood. These antibodies are anti-CD 71, anti-CD 36, and anti-GPA. Anti-CD 71 binds the transferrin receptor, CD-36 binds the thrombospondin receptor (hormone receptor), while anti-GPA binds glycophorin A. See page 294 4th paragraph. Blood samples were collected from pregnant women between 8 and 19 weeks gestation (within the first trimester). See page 295 1st paragraph.

The method is cells were isolated/separated by antibody binding and analyzed via flow cytometry, sorting, and PCR. See page 295 through 296. The results showed that the GPA (red cell-specific antigen) allowed for the separation of fetal nucleated erythroid cells from maternal blood. See page 299 last paragraph.

Bianchi et al. differs from the instant invention in failing to teach a method of identifying and isolating embryonic or fetal red blood cells via an adult liver component that is cell surface exposed.

It is noted that the specification teaches that glucose-6-phosphase is an adult liver component meeting the limitations of the claims. (Page 8 section 0047). The references to Hume et al. disclose the use of antibodies to glucose-6-phosphase.

Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) show that the microsomal glucose-6-phosphatase enzyme protein is expressed in human embryonic and fetal red blood cells. Glucose-6-phosphatase was found to be immunopositive for circulating red cells in the primitive megaloblastic series.

Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) et al. teaches that microsomal glucose-6-phosphatase catalyzes the terminal step of glycogenolysis and gluconeogenesis and is expressed predominantly in the liver. The study of the endoplasmic reticulum system involving glucose-6-phosphatase, lead investigators to study other endoplasmic reticulum proteins. These proteins included uridine diphosphate-glucuronosyltransferase, cytochrome P450 isozymes, nicotinamide adenine dinucleotide phosphatecytochrome P450 oxidoreductase, and prostaglandin H synthase.

Bianchi et al., Hume et al., and Hume et al., are all analogous art because they are from the same field of endeavor, all three inventions teach immunoassay techniques involving fetal red blood cells and prenatal diagnosis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the specific proteins relating to microsomal glucose-6-phosphatase as taught by Hume et al., and Hume et al. in the methods of Bianchi et al. to perform fetal red blood cell identification, isolation, and assay techniques, because Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) taught that the predominantly hepatic protein (glucose-6-phosphatase) in adults is present in nucleated embryonic and fetal red blood cells and is useful in diagnosis of disorders associated with liver protein expression in the first trimester maternal circulation.

While, Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) taught that expression of these key enzymes (glucose-6-phosphatase) in early fetal RBCs provides a means for the study of fetal development in these areas. See abstract.

One having ordinary skill in the art would have been motivated to do this because the early detection of such disorders is both beneficial in possible treatment and early preparation/education of the fetal family for the birth of an abnormal baby.

With respect to claim 7 wherein the concentration of the detectable adult liver component is at less than 1 percent per cell basis in maternal cells. Such detection limits are viewed as mere assay optimization. Absent results to the contrary or unexpected results the modification is viewed as an obvious modification that does not render the claims patentably distinct from the prior art assay methods.

II. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al. (Prenatal Diagnosis, Vol.13, 293-300, 1993) in view of Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) and Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) as applied to claims 2, 5-7, 9 and 14-15 above, and further in view of in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Please see Bianchi et al. in view of Hume et al. and Hume et al. as set forth above.

Bianchi et al. in view of Hume et al. and Hume et al. differ from the instant invention in not specifically teaching reagent immobilization to a solid support such as micro titer plates.

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize the reagents on a solid support/micro titer plates as taught by Maggio in the assay method to isolate red blood cells of Bianchi et al. in view of Hume et al. and Hume et al. because Maggio taught that micro plates or micro titer plates "are very convenient for reagent immobilization and eliminate washing thereby reducing labor in assay procedures". Page 186, last line.

Response to Arguments

5. Applicant contends that the prior art teaches the detection of glucose-6-phosphatase (adult liver component) but this does not make the method of isolating embryonic/fetal cells obvious because glucose-6-phosphatase (adult liver component) is not a cell surface exposed component. This argument was carefully considered but not found persuasive because the instant specification teaches glucose-6-phosphatase on page 7 section 0037 through 0040 and page 8 section 0047 through page 9 section 0048.

The claims recite a cell surface exposed component and does not define that this is meant to read on extracelluar expression of the protein therefore glucose-6-phosphatase meets the limitations of the instantly recited claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., intracellular or extracelluar protein expression) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Further, glucose-6-phospatase is a "cell surface exposed component" because it can be exposed for visual identification and cell isolation as supported in the references of Hume et al. (1995 –page 87-88 Cell Counting/1996 –page 763 Cell Counting) and on the specification (page 10 section 0058).

Applicant also contends that glucose-6-phosphatase is not one of the components in the Markush group of claim 9. This argument was carefully considered but not found persuasive because the reference of Hume et al. (1996 –Abstract) discloses that not only glucose-6-phosphatase but other components of the glucose-6-phosphatase system are expressed in embryonic and fetal RBC precursors. GLUT2 of claim 9, is a known component of the glucose-6-phosphastase system and would therefore be an obvious component to measure (For example see Burchell et al., Molecular Membrane Biology, 1994, 11, 217-227). The test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the pertinent art. See *In re Bent,* 52 CCPA 850, 144 USPQ 28 (1964); *In re Nievelt,* 179 USPQ 224 (CCPA 1973). A reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. *In re Boe,* 355 F.2d 961, 148 USPQ 507 (CCPA 1966). *In re Chapman,* 357 F.2d 418, 148 USPQ 711 (CCPA 1966).

In response to the argument that the rejection of claim 13 in further view of Maggio is not obvious by virtue of its dependency on amended claims 2 and 9, it is noted that the primary references have been addressed above. Accordingly the rejection of claim 13 is maintained.

6. For reasons aforementioned, no claims are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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